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Extract

of  
Hypericum  
perforatum

used to treat  
a health disorder

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NOTE TO EXAMINER

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25

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wherein

R<sub>1</sub> is H, OH, OR or OCOR;

R<sub>2</sub> is H, R, F, Cl, Br, I or SO<sub>3</sub>H;

R<sub>3</sub> is H, R, OH, OR, OCOR, CH<sub>2</sub>OH, CH<sub>2</sub>OR, CH<sub>2</sub>OCOR, COOH or COOR;

R<sub>4</sub> is H, R, OH, OR, OCOR, CH<sub>2</sub>OH, CH<sub>2</sub>OR, CH<sub>2</sub>OCOR, COOH or COOR;

R<sub>5</sub> is H, R, F, Cl, Br, I or SO<sub>3</sub>H;

R<sub>6</sub> is H, OH, OR or OCOR;

R<sub>7</sub> is H, OH, OR or OCOR;

R<sub>8</sub> is H, R, F, Cl, Br, I or SO<sub>3</sub>H;

R<sub>9</sub> is H, R, OH, OR, OCOR, CH<sub>2</sub>OH, CH<sub>2</sub>OR, CH<sub>2</sub>OCOR, COOH or COOR;

R<sub>10</sub> is H, R, OH, OR, OCOR, CH<sub>2</sub>OH, CH<sub>2</sub>OR, CH<sub>2</sub>OCOR, COOH or COOR;

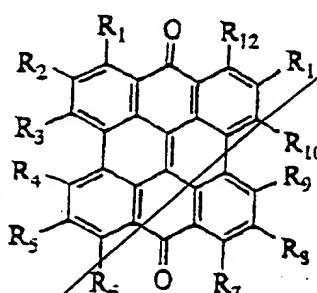
R<sub>11</sub> is H, R, F, Cl, Br, I or SO<sub>3</sub>H;

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group

What is claimed is:

1. A method of treating a health disorder treatable with a T-type calcium channel blocker in an animal in need of such a treatment, comprising administering an effective amount of an active agent to said animal, wherein said active agent is Hypericum perforatum, a Hypericum extract, an extract of a species of the Hypericum genus other than Hypericum perforatum, a Hypericum constituent, a hypericin derivative or a hypericin analog, with the proviso that when the active agent is Hypericum perforatum or Hypericum extract, said health disorder is not depression or migraine headache.

2. The method of claim 1, wherein said hypericin derivative is a compound of formula II,



II

wherein

R<sub>1</sub> is H, OH, OR or OCOR;

R<sub>2</sub> is H, R, F, Cl, Br, I or SO<sub>3</sub>H;

R<sub>3</sub> is H, R, OH, OR, OCOR, CH<sub>2</sub>OH, CH<sub>2</sub>OR, CH<sub>2</sub>OCOR, COOH or COOR;

R<sub>4</sub> is H, R, OH, OR, OCOR, CH<sub>2</sub>OH, CH<sub>2</sub>OR, CH<sub>2</sub>OCOR, COOH or COOR;

R<sub>5</sub> is H, R, F, Cl, Br, I or SO<sub>3</sub>H;

R<sub>6</sub> is H, OH, OR or OCOR;

R<sub>7</sub> is H, OH, OR or OCOR;

R<sub>8</sub> is H, R, F, Cl, Br, I or SO<sub>3</sub>H;

R<sub>9</sub> is H, R, OH, OR, OCOR, CH<sub>2</sub>OH, CH<sub>2</sub>OR, CH<sub>2</sub>OCOR, COOH or COOR;

R<sub>10</sub> is H, R, OH, OR, OCOR, CH<sub>2</sub>OH, CH<sub>2</sub>OR, CH<sub>2</sub>OCOR, COOH or COOR;

R<sub>11</sub> is H, R, F, Cl, Br, I or SO<sub>3</sub>H;

$R_{12}$  is H, OH, OR or OCOR; and

R is an optionally substituted  $C_1$ - $C_{30}$  alkyl group;

with the proviso that the following compounds are excluded

(A) a compound of formula II, wherein  $R_1$ ,  $R_3$ ,  $R_4$ ,  $R_6$ ,  $R_7$  and  $R_{12}$  are OH,  $R_2$ ,  $R_5$ ,  $R_8$  and  $R_{11}$  are H, and  $R_9$  and  $R_{10}$  are methyl;

5 (B) a compound of formula II, wherein  $R_1$ ,  $R_9$ ,  $R_{10}$ ,  $R_6$ ,  $R_7$  and  $R_{12}$  are OH,  $R_2$ ,  $R_5$ ,  $R_8$  and  $R_{11}$  are H, and  $R_3$  and  $R_4$  are methyl;

(C) a compound of formula II, wherein  $R_1$ ,  $R_3$ ,  $R_4$ ,  $R_6$ ,  $R_7$  and  $R_{12}$  are OH,  $R_2$ ,  $R_5$ ,  $R_8$  and  $R_{11}$  are H,  $R_9$  is methyl, and  $R_{10}$  is  $CH_2OH$ ;

10 (D) a compound of formula II, wherein  $R_1$ ,  $R_3$ ,  $R_4$ ,  $R_6$ ,  $R_7$  and  $R_{12}$  are OH,  $R_2$ ,  $R_5$ ,  $R_8$  and  $R_{11}$  are H,  $R_9$  is  $CH_2OH$  and  $R_{10}$  is methyl;

(E) a compound of formula II, wherein  $R_1$ ,  $R_9$ ,  $R_{10}$ ,  $R_6$ ,  $R_7$  and  $R_{12}$  are OH,  $R_2$ ,  $R_5$ ,  $R_8$  and  $R_{11}$  are H,  $R_3$  is methyl, and  $R_4$  is  $CH_2OH$ ; and

(F) a compound of formula II, wherein  $R_1$ ,  $R_9$ ,  $R_{10}$ ,  $R_6$ ,  $R_7$  and  $R_{12}$  are OH,  $R_2$ ,  $R_5$ ,  $R_8$  and  $R_{11}$  are H,  $R_3$  is  $CH_2OH$  and  $R_4$  is methyl.

3. The method of claim 1, wherein the health disorder treatable with T-type calcium channel blockers is depression, chronic heart failure, congestive heart failure, ischaemic condition, arrhythmia, angina pectoris, hypertension, hypoinsulinemia, hyperinsulinemia, diabetes mellitus, hyperaldosteronemia, epilepsy, migraine headache, brain aging, a neurodegenerative disease or preterm labor. *Excluded in 1, last*

4. The method of claim 1, wherein said Hypericum constituent is hypericin, pseudohypericin, hyperforin, ashyperforin, quercetin, quercitrin, isoquercitrin, hyperoside, rutin, amentoflavone or hyperin.

25 5. The method of claim 2, wherein R is a  $C_1$ - $C_{30}$  alkyl group, optionally substituted with one to three substituents independently selected from hydroxy, alkoxy, acyloxy, carboxy, alkoxycarbonyl, amino, alkylamino, dialkylamino, nitro or phenyl group or fluorine, chlorine, bromine or iodine atom.

30 6. The method of claim 5, wherein

$R_1$  is H, OH, OR or OCOR;

$R_2$  is H or R;

$R_3$  is H, OH, OR, OCOR,  $CH_2OH$ ,  $CH_2OR$  or  $CH_2OCOR$ ;

$R_4$  is H, OH, OR, OCOR,  $CH_2OH$ ,  $CH_2OR$  or  $CH_2OCOR$ ;

$R_5$  is H or R;

$R_6$  is H, OH, OR or OCOR;

$R_7$  is H, OH, OR or OCOR;

5        $R_8$  is H or R;

$R_9$  is H, OH, OR, OCOR,  $CH_2OH$ ,  $CH_2OR$  or  $CH_2OCOR$ ;

$R_{10}$  is H, OH, OR, OCOR,  $CH_2OH$ ,  $CH_2OR$  or  $CH_2OCOR$ ;

$R_{11}$  is H or R;

$R_{12}$  is H, OH, OR or OCOR; and

10       R is an optionally substituted  $C_1$ - $C_6$  alkyl group.

7.       The method of claim 6, wherein R is an optionally substituted methyl or ethyl group.

8.       The method of claim 1, wherein said animal is a human.

9.       The method of claim 1, wherein said active agent is a Hypericum

15       extract.

10.       The method of claim 9, wherein said effective amount is about 0.05 mg to 500 mg per kg body weight of said animal.

11.       The method of claim 1, wherein said active agent is hypericin.

12.       The method of claim 11, wherein said effective amount is about 20       0.0015 mg to 15 mg per kg body weight of said animal.

13.       The method of claim 1, further comprising administering to said animal an additional active agent as described in claim 1.

14.       The method of claim 13, wherein one of the active agents administered is hypericin.

25       15.       The method of claim 14, wherein another of the active agents administered is pseudohypericin.

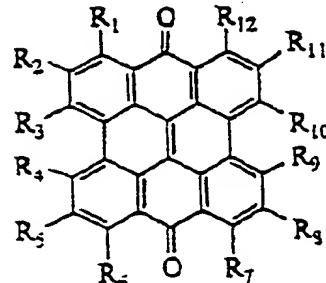
16.       The method of claim 14, wherein another of the active agents administered is hyperforin.

30       17.       The method of claim 15, further comprising administering hyperforin to said animal.

## 18. A compound of formula II,

5

wherein



II

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$R_1$  is H, OH, OR or OCOR;  
 $R_2$  is H, R, F, Cl, Br, I or  $SO_3H$ ;

$R_3$  is H, R, OH, OR, OCOR,  $CH_2OH$ ,  $CH_2OR$ ,  $CH_2OCOR$ , COOH or COOR;

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$R_4$  is H, R, OH, OR, OCOR,  $CH_2OH$ ,  $CH_2OR$ ,  $CH_2OCOR$ , COOH or COOR;

$R_5$  is H, R, F, Cl, Br, I or  $SO_3H$ ;

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$R_6$  is H, OH, OR or OCOR;  
 $R_7$  is H, OH, OR or OCOR;  
 $R_8$  is H, R, F, Cl, Br, I or  $SO_3H$ ;

$R_9$  is H, R, OH, OR, OCOR,  $CH_2OH$ ,  $CH_2OR$ ,  $CH_2OCOR$ , COOH or COOR;

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$R_{10}$  is H, R, OH, OR, OCOR,  $CH_2OH$ ,  $CH_2OR$ ,  $CH_2OCOR$ , COOH or COOR;

$R_{11}$  is H, R, F, Cl, Br, I or  $SO_3H$ ;

$R_{12}$  is H, OH, OR or OCOR; and

$R$  is an optionally substituted  $C_1-C_{30}$  alkyl group;

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with the proviso that the following compounds are excluded

(A) a compound of formula II, wherein  $R_1$ ,  $R_3$ ,  $R_4$ ,  $R_6$ ,  $R_7$  and  $R_{12}$  are OH,  $R_2$ ,  $R_5$ ,  $R_8$  and  $R_{11}$  are H, and  $R_9$  and  $R_{10}$  are methyl;

(B) a compound of formula II, wherein  $R_1$ ,  $R_9$ ,  $R_{10}$ ,  $R_6$ ,  $R_7$  and  $R_{12}$  are OH,  $R_2$ ,  $R_5$ ,  $R_8$  and  $R_{11}$  are H, and  $R_3$  and  $R_4$  are methyl;

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(C) a compound of formula II, wherein  $R_1$ ,  $R_3$ ,  $R_4$ ,  $R_6$ ,  $R_7$  and  $R_{12}$  are OH,  $R_2$ ,  $R_5$ ,  $R_8$  and  $R_{11}$  are H,  $R_9$  is methyl, and  $R_{10}$  is  $CH_2OH$ ;

(D) a compound of formula II, wherein  $R_1$ ,  $R_3$ ,  $R_4$ ,  $R_6$ ,  $R_7$  and  $R_{12}$  are OH,  $R_2$ ,  $R_5$ ,  $R_8$  and  $R_{11}$  are H,  $R_9$  is  $CH_2OH$  and  $R_{10}$  is methyl;

(E) a compound of formula II, wherein R<sub>1</sub>, R<sub>9</sub>, R<sub>10</sub>, R<sub>6</sub>, R<sub>7</sub> and R<sub>12</sub> are OH, R<sub>2</sub>, R<sub>5</sub>, R<sub>8</sub> and R<sub>11</sub> are H, R<sub>3</sub> is methyl, and R<sub>4</sub> is CH<sub>2</sub>OH;

(F) a compound of formula II, wherein R<sub>1</sub>, R<sub>9</sub>, R<sub>10</sub>, R<sub>6</sub>, R<sub>7</sub> and R<sub>12</sub> are OH, R<sub>2</sub>, R<sub>5</sub>, R<sub>8</sub> and R<sub>11</sub> are H, R<sub>3</sub> is CH<sub>2</sub>OH and R<sub>4</sub> is methyl.

5 19. The compound of claim 18, wherein R is a C<sub>1</sub>-C<sub>30</sub> alkyl group, optionally substituted with one to three substituents independently selected from hydroxy, alkoxy, acyloxy, carboxy, acoxycarbonyl, amino, alkylamino, dialkylamino, nitro or phenyl group or fluorine, chlorine, bromine or iodine atom.

10 20. The compound of claim 18, wherein

R<sub>1</sub> is H, OH, OR or OCOR;

R<sub>2</sub> is H or R;

R<sub>3</sub> is H, OH, OR, OCOR, CH<sub>2</sub>OH, CH<sub>2</sub>OR or CH<sub>2</sub>OCOR;

R<sub>4</sub> is H, OH, OR, OCOR, CH<sub>2</sub>OH, CH<sub>2</sub>OR or CH<sub>2</sub>OCOR;

15 R<sub>5</sub> is H or R;

R<sub>6</sub> is H, OH, OR or OCOR;

R<sub>7</sub> is H, OH, OR or OCOR;

R<sub>8</sub> is H or R;

R<sub>9</sub> is H, OH, OR, OCOR, CH<sub>2</sub>OH, CH<sub>2</sub>OR or CH<sub>2</sub>OCOR;

20 R<sub>10</sub> is H, OH, OR, OCOR, CH<sub>2</sub>OH, CH<sub>2</sub>OR or CH<sub>2</sub>OCOR;

R<sub>11</sub> is H or R;

R<sub>12</sub> is H, OH, OR or OCOR; and

R is an optionally substituted C<sub>1</sub>-C<sub>6</sub> alkyl group.

21. The compound of claim 20, wherein R is an optionally substituted methyl or ethyl group

22. The method of claim 1, wherein said extract of a species of the *Hypericum* genus other than *Hypericum perforatum* is an extract of a species selected from the group consisting of *H. majus*, *H. formosum*, *H. calycinum*, *H. X moseranum*, *H. irazuense*, *H. reductum*, *H. patulum*, *H. mutilum*, *H. crux-andreae*, *H. hypericoides*, *H. densiflorum*, *H. prolificum*, *H. frondosum*, *H. cumilicola*, *H. anagalloides*, *H. androsaemum*, *H. tetrapterum*, *H. hirsutum*, *H. olympicum*, *H. hyssopifolium*, *H. elongatum* and *H. erratum*.

add  
C3